	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	229	(dipeptidyl adj peptidase adj IV) or (DP adj IV)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:16			0
2	BRS	L2	95	l1 same inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:29			0
3	BRS	L3	5	l2 same unstable	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:17			0
4	BRS	L4	2	2 same masked	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:30			0
5	BRS	L5	3	(Ile-thia) or (ile-pyr) or (val-thia) or (val-pyr)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:31			0
6	BRS	L6	1	(dipeptidyl adj alkyl adj ketone) or (dipeptidyl adj fluoroalkyl adj ketone) or (dipeptidyl adj chloroalkyl adj ketone) or (dipeptidyl adj cyanide) or (dipeptidyl adj pyridium adj methyl adj ketone)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:35			0
7	BRS	L7	2938	(alkyl adj ketone) or (fluoroalkyl adj ketone) or (chloroalkyl adj ketone) or (dipeptidyl adj cyanide) or (pyridium adj methylketone)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:36			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
8	BRS	L8	2	1 same 7	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:37			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	229	(dipeptidyl adj peptidase adj IV) or (DP adj IV)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:55			0
2	BRS	L2	95	((dipeptidyl adj peptidase adj IV) or (DP adj IV)) same inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:55			0
3	BRS	L3	21	2 same diabetes	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/05/20 14:56			0

> d his

(FILE 'HOME' ENTERED AT 14:41:12 ON 20 MAY 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
14:41:55 ON 20 MAY 2002
L1 5851 S (DIPEPTIDYL PEPTIDASE IV) OR (DP-IV) OR (DPP-IV)
L2 1752 S L1 (P) INHIBIT?
L3 14 S L2 (P) UNSTABLE
L4 5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)
L5 5 S (ILE-THIA) OR (ILE-PYR) OR (VAL-THIA) OR (VAL-PYR)
L6 5 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)
L7 0 S L6 (P) L1
L8 5 S L6 NOT L4
L9 166 S ALKYLKETONE OR (FLUOROALKYL KETONE) OR (CHLOROALKYL KETONE) O
L10 0 S L1 AND L9
L11 1 S L9 AND DIPEPTID?
L12 1 S L11 NOT L4
L13 158 S L2 (P) DIABETES
L14 66 DUPLICATE REMOVE L13 (92 DUPLICATES REMOVED)
L15 0 S L9 AND L14
L16 0 S L13 AND MASKED
L17 0 S L9 AND DIABETES

=> log y

FILE 'MEDLINE' ENTERED AT 14:41:5 N 20 MAY 2002

FILE 'CAPLUS' ENTERED AT 14:41:55 ON 20 MAY 2002

FILE 'BIOSIS' ENTERED AT 14:41:55 ON 20 MAY 2002

FILE 'EMBASE' ENTERED AT 14:41:55 ON 20 MAY 2002

FILE 'SCISEARCH' ENTERED AT 14:41:55 ON 20 MAY 2002

FILE 'AGRICOLA' ENTERED AT 14:41:55 ON 20 MAY 2002

=> s (dipeptidyl peptidase IV) or (DP-IV) or (DPP-IV)
L1 5851 (DIPEPTIDYL PEPTIDASE IV) OR (DP-IV) OR (DPP-IV)

=> s l1 (p) inhibit?
L2 1752 L1 (P) INHIBIT?

=> s l2 (p) unstable
L3 14 L2 (P) UNSTABLE

=> duplicate remove l3
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L3
L4 5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)

=> d l4 1-5 ibib abs

L4 ANSWER 1 OF 5 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001410442 MEDLINE
DOCUMENT NUMBER: 21235368 PubMed ID: 11337057
TITLE: Transbuccal peptide delivery: stability and in vitro permeation studies on endomorphin-1.
AUTHOR: Bird A P; Faltinek J R; Shojaei A H
CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of Pharmacy, Texas Tech University Health Sciences Center, Amarillo, TX 79106, USA.
SOURCE: JOURNAL OF CONTROLLED RELEASE, (2001 May 18) 73 (1) 31-6. Journal code: C46; 8607908. ISSN: 0168-3659.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010723
Last Updated on STN: 20010723
Entered Medline: 20010719

AB The purpose of this study was to investigate the feasibility of buccal delivery of a model peptide, endomorphin-1 (ENI), using stability and in vitro permeation studies. ENI is a recently isolated mu-opiate receptor agonist with high selectivity and specificity for this receptor subtype. Stability studies were conducted in various buffers and the drug was shown to be stable in both acidic and basic buffer systems. In the presence of full thickness porcine buccal epithelium, ENI was ***unstable*** with only 23.4+/-15.7% intact drug present after 6 h. The region responsible for this degradation was found to coincide with the major barrier region of the buccal epithelium as delineated through stability experiments in the presence of partial thickness buccal epithelium. Various peptidase ***inhibitors*** were used to isolate the enzyme(s) responsible for this degradation. Diprotin-A, a potent ***inhibitor*** of ***dipeptidyl*** ***peptidase*** ***IV*** , provided significant ***inhibition*** of the degradation of ENI in the presence of buccal epithelium. In vitro permeation studies revealed that the permeability coefficient of ENI across porcine buccal epithelium was 5.67+/-4.74x10(-7)

cm/s. The enzymatic degradation of ENI was found not to be rate limiting to the drug's permeation acr[redacted] buccal epithelium, as diproti[redacted] did not increase the permeation of ENI. Sodium glycocholate as well as sodium taurocholate were also ineffective in enhancing the permeation of ENI across porcine buccal epithelium.

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:819402 CAPLUS
DOCUMENT NUMBER: 132:36038
TITLE: Synthesis of prodrugs of ***unstable*** ***dipeptidyl*** ***peptidase*** ***IV*** ***inhibitors*** for use in treating diabetes
INVENTOR(S): Demuth, Hans-Ulrich; Schmidt, Jorn; Hoffmann, Torsten; Glund, Konrad
PATENT ASSIGNEE(S): Probiodrug Gesellschaft Fur Arzneimittelforschung m.b.H., Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9967279	A1	19991229	WO 1999-EP4381	19990624
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19828114	A1	20000127	DE 1998-19828114	19980624
AU 9947772	A1	20000110	AU 1999-47772	19990624
BR 9911415	A	20010320	BR 1999-11415	19990624
EP 1090030	A1	20010411	EP 1999-931163	19990624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2000006483	A	20001219	NO 2000-6483	20001219
US 2001020006	A1	20010906	US 2000-745883	20001221

PRIORITY APPLN. INFO.: DE 1998-19828114 A 19980624
WO 1999-EP4381 W 19990624

OTHER SOURCE(S): MARPAT 132:36038
GI

/ Structure 1 in file .gra /

AB The invention relates to compds. of ***unstable*** ***inhibitors*** of ***dipeptidyl*** ***peptidase*** ***IV*** (***DP*** ***IV***) which comprise general formula A-B-C, whereby A represents an amino acid, B represents the chem. bond between A and C or an amino acid, and C represents an ***unstable*** ***inhibitor*** of ***DP*** ***IV*** . Such compds. are used for treating altered glucose tolerance, glucosuria, hyperlipidemia, metabolic acidosis, diabetes mellitus, diabetic neuropathy, nephropathy, and secondary diseases in mammals caused by diabetes mellitus. Thus, (I) was reacted with pyridine to give [(II); R = Cbz], which was deprotected to give II (R = H)(III) which is thought to undergo an intramol. cyclization (no data) to form the active ***DP*** ***IV*** ***inhibitor*** . In 0.1 M HEPES-buffer, pH 7.6, at 25.degree., III had a half life (before self-cyclization) of 13.3 min.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 5 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1998327123 MEDLINE
DOCUMENT NUMBER: 98327123 PubMed ID: 9660870
TITLE: Functional specialization of stable and dynamic microtubules in protein traffic in WIF-B cells.
AUTHOR: Pous C; Chabin K; Drechou A; Barbot L; Phung-Koskas T; Settegrana C; Bourguet-Kondracki M L; Maurice M; Cassio D; Guyot M; Durand G
CORPORATE SOURCE: Laboratoire de Biochimie Generale, Equipe d'Accueil 1595, Unite de Formation et de Recherche de Pharmacie, Universite Paris-Sud, 92296 Chatenay-Malabry, France.
SOURCE: JOURNAL OF CELL BIOLOGY, (1998 Jul 13) 142 (1) 153-65. Journal code: HMV; 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 19980828
Entered Medline: 19980820

AB We found that the magnesium salt of ilimaquinone, named 201-F, specifically disassembled dynamically ***unstable*** microtubules in fibroblasts and various epithelial cell lines. Unlike classical tubulin-interacting drugs such as nocodazole or colchicine which affect all classes of microtubules, 201-F did not depolymerize stable microtubules. In WIF-B-polarized hepatic cells, 201-F disrupted the Golgi complex and ***inhibited*** albumin and alpha1-antitrypsin secretion to the same extent as nocodazole. By contrast, 201-F did not impair the transport of membrane proteins to the basolateral surface, which was only affected by the total disassembly of cellular microtubules. Transcytosis of two apical membrane proteins-the alkaline phosphodiesterase B10 and ***dipeptidyl*** ***peptidase*** ***IV*** -was affected to the same extent by 201-F and nocodazole. Taken together, these results indicate that only dynamically ***unstable*** microtubules are involved in the transport of secretory proteins to the plasma membrane, and in the transcytosis of membrane proteins to the apical surface. By contrast, stable microtubules, which are not functionally affected by 201-F treatment, are involved in the transport of membrane proteins to the basolateral surface. By specifically disassembling highly dynamic microtubules, 201-F is an invaluable tool with which to study the functional specialization of stable and dynamic microtubules in living cells.

L4 ANSWER 4 OF 5 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95220827 EMBASE
DOCUMENT NUMBER: 1995220827
TITLE: Amino acid and peptide phosphonate derivatives as specific inhibitors of serine peptidases.
AUTHOR: Oleksyszyn J.; Powers J.C.
CORPORATE SOURCE: OsteoArthritis Sciences, Inc.,Cambridge, MA 02139, United States
SOURCE: Methods in Enzymology, (1994) 244/- (423-441). ISSN: 0076-6879 CODEN: MENZAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters have a number of advantages for in vitro and in vivo experiments compared to other commonly used peptide serine peptidase ***inhibitors*** . They are easily synthesized, are chemically very stable, and are not alkylating agents such as the commonly used peptide chloromethyl ketone serine peptidase ***inhibitors*** . They are more stable than most other organophosphorus ***inhibitors*** , including peptidyl derivatives of the .alpha.-aminoalkyl phosphonates, where the phosphonate moiety is chemically activated by the presence of better leaving groups. The .alpha.-aminoalkyl phosphonate diphenyl esters have outstanding stability (t(1/2) usually greater than 4 days at pH 7.5; >24 hr in plasma). Thus, low ***inhibitor*** concentrations can effectively control unwanted serine peptidase activity with low ***inhibitor*** concentrations over long time periods, which makes them perfect tools for experiments

involving cells. Because .alpha.-aminoalkyl phosphonate diphenyl esters are irreversible ***inhibitors*** , they offer real advantages in many experimental situations over reversible ***inhibitors*** In cases in which it may be necessary to maintain high concentrations of the reversible ***inhibitor*** for long time periods. The second-order ***inhibition*** rate constants for phosphonate ***inhibitors*** are usually not as high as those observed with other types of peptidyl serine peptidase ***inhibitors*** . This is compensated for by their high stability and specificity. The irreversible character of the ***inhibition*** reaction allows effective ***inhibition*** even if the inactivation rate constant is not large. For example, Cbz-Val(P)(OPh)2 ***inhibits*** HLE with a rate constant of 260 M-1 sec-1. Thus at an effective concentration of 10 .mu.M, 50% of the enzyme is inactivated after 4.5 min, and almost no activity is detected after an 11-min incubation time. Frequently there is a need to specifically ***inhibit*** serine peptidases in vitro during protein purification procedures or in biological experiments involving cells or tissue culture. Typically, peptide chloromethyl ketone derivatives are used. However, these inactivators are quite nonspecific alkylating agents and experimental results can be misleading. For example, the presence of a chymotrypsin-like enzyme activity on the neutrophil membrane was assumed when ***inhibition*** with Tos-Phe-CH2Cl resulted in ***inhibition*** of the so-called oxidative burst of these cells. However, it has been shown that the targeted protein is not a serine peptidase, and ***inhibition*** results from a nonspecific alkylation reaction. As another example of the utility of phosphonates, dipeptide derivatives of .alpha.-aminoalkyl phosphonate diphenyl ester derivatives with a P1 proline residue are effective ***inhibitors*** for ***dipeptidyl*** - ***peptidase*** ***IV*** . The corresponding dipeptide boronic acid and chloromethyl ketone derivatives are ***unstable*** . In summary, peptidyl derivatives of .alpha.-aminoalkyl phosphonate diphenyl esters are highly specific irreversible ***inhibitors*** of serine peptidases and are chemically stable and stable in plasma. They offer a number of advantages over other types of ***inhibitors*** currently in use in biological experiments. After reaction with the enzyme, they form very stable enzyme- ***inhibitor*** complexes, making them interesting tools for X-ray studies on the active site structure of new serine peptidases.

L4 ANSWER 5 OF 5 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 79215750 MEDLINE
DOCUMENT NUMBER: 79215750 PubMed ID: 457448
TITLE: [Peptidases II. Localization of dipeptidylpeptidase IV (DPP IV). Histochemical and biochemical study].
Peptidasen II. Zur Lokalisation der Dipeptidylpeptidase IV (DPP IV). Histochemische und biochemische Untersuchung.
AUTHOR: Gossrau R
SOURCE: HISTOCHEMISTRY, (1979 Apr 3) 60 (2) 231-48.
Journal code: G9K; 0411300. ISSN: 0301-5564.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197909
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 20000303
Entered Medline: 19790917

AB Fresh frozen, unfixed, chloroforme-acetone treated or freeze-dried cryostat sections or sections from aldehyde-fixed blocks of tissue were tried for the histochemical investigation of dipeptidylpeptidase IV (***DPP*** ***IV***) with L-glycyl-L-prolyl(gly-pro)-naphthylamides as substrates and stable or ***unstable*** diazonium salts for simultaneous coupling and various buffers, pH 5--7.5 in rats, mice, guinea-pigs, cats, rabbits, hamsters and human enterobiopsies. The best results are obtained with 1.7--3.4 mM gly-pro-4-methoxy-2-naphthylamide and 1 mg Fast Blue B/ml or (with some limitations) 0.025 ml hexazotized new fuchsine/ml in 0.1 M cacodylate or phosphate buffer, pH 7.5 and unfixed sections for the demonstration of the total activity of ***DPP*** ***IV*** and freeze-dried celloidin-mounted cryostat sections for the precise localization of the enzyme or the detection of lysosomes, Golgi apparatus and secretion granules sections from aldehyde fixed tissue blocks are only suitable to study the lysosomal hydrolysis of

gly-pro-naphthylamides between pH 5 and 7 when hexazotized p-rosaniline or new fuchsine are employed. ***DPP*** ***IV*** is firmly bound to strutures and shows species- and organ-dependent differences. In general, the enzyme occurs in the capillary endothelium, sinusoidal cells, perineurium, epithelial cells of intercalated and striated ducts, microvillous zone of intestinal crypts and villi, uterus, Fallopian tubes, ductus epididymis and proximal renal tubules, hepatocyte and lymphocyte membrane, plasmalemma of pseudostratified and transient epithelia and in the capsules and interstitium of many organs. These sites of activity can be completely ***inhibited*** by diisopropyl fluorophosphate and partially by Pb2+; Mg2+, Mn2+, Co2+ EDTA are without any influence. Phenantrolin may activate ***DPP*** ***IV*** . The biochemical assay works with 10 mM gly-pro-2-naphthylamide in 0.1 M cacodylate buffer, pH 7; the enzyme activity is determined fluorometrically in guinea-pig and rat organs; the data confirm and enlarge the species- and organ-dependent differences revealed by histochemistry. Compared with other dipeptide as well as tripeptide and amino acid naphthylamides the results obtained for ***DPP*** ***IV*** suggest a peptidylpeptidase which seems to be involved in other metabolic processes beside the degradation of collagen.

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=> d his

     (FILE 'HOME' ENTERED AT 14:41:12 ON 20 MAY 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     14:41:55 ON 20 MAY 2002
L1          5851 S (DIPEPTIDYL PEPTIDASE IV) OR (DP-IV) OR (DPP-IV)
L2          1752 S L1 (P) INHIBIT?
L3            14 S L2 (P) UNSTABLE
L4             5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)

=> s (ile-thia) or (ile-pyr) or (val-thia) or (val-pyr)
L5             5 (ILE-THIA) OR (ILE-PYR) OR (VAL-THIA) OR (VAL-PYR)

=> duplicate remove l5
PROCESSING COMPLETED FOR L5
L6             5 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)

=> s l6 (p) l1
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L31 (P) L1'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L35 (P) L3'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L37 (P) L4'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L39 (P) L5'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L41 (P) L6'
L7             0 L6 (P) L1

=> s l6 not l4
L8             5 L6 NOT L4

=> d l8 1-5 ibib abs

L8   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         1970:62931  CAPLUS
DOCUMENT NUMBER:          72:62931
TITLE:                    Pyrrolidonecarboxylyl peptidase from rat liver
AUTHOR(S):                Armentrout, Richard W.
CORPORATE SOURCE:         Univ. of California, La Jolla, Calif., USA
SOURCE:                   Biochim. Biophys. Acta (1969), 191(3), 756-9
                          CODEN: BBACAQ
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Pyrrolidone-carboxylyl (Pyr) peptidase (I) was partially purified from rat
     liver (RL) and compared with bacterial (B) I.  The sizes of the RL and B
     enzymes were compared by Sephadex G-200 chromatog.  The RL I behaved as
     though it had a significantly smaller radius than the B I.  The 2 enzymes
     behaved similarly during purification.  Both contained SH groups.  The RL
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I was extremely sensitive to inactivation in the absence of a reducing agent, and in this respect differed from B I. Both RL and B [illegible]repns. were stabilized, as well as reversibly inhibited, by 2-pyrrolidone. Both enzymes hydrolyzed certain dipeptides in the same order of rate, i.e. Pyr-Ala > Pyr- ***Ile*** > ***Pyr*** -Phe. Therefore RL contains a I activity similar to B I with respect to purification, requirement for a reducing environment, stabilization and inhibition by 2-pyrrolidone, order of reaction rate with certain peptides, and specificity. The RL I can specifically remove the pyrrolidone carboxylyl residue from bovine fibrinopeptide B without detectable attack on the remainder of the mol.

L8 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1969:400281 CAPLUS
DOCUMENT NUMBER: 71:281
TITLE: Pyrrolidonecarboxylyl peptidase: specificity of the enzyme
AUTHOR(S): Uliana, Joseph A.; Doolittle, Russell F.
CORPORATE SOURCE: Univ. of California, La Jolla, Calif., USA
SOURCE: Arch. Biochem. Biophys. (1969), 131(2), 561-5
CODEN: ABBIA4
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A variety of pyrrolidonecarboxylyl dipeptides were synthesized in order to study the specificity of pyrrolidonecarbox-ylyl (Pyr) peptidase, a hydrolytic enzyme isolated from a strain of Pseudomonas fluorescens. The influence of the penultimate amino acid (nearest neighbor to the pyrrolidonecarboxylyl residue) on the rate of hydrolysis of L-pyrrolidonecarboxylyl-L-amino acid dipeptides was quite large. The order of relative hydrolysis rates varied in the following sequence: pyr-Ala > Pyr-Ilu > Pyr- ***Val*** > ***Pyr*** -Leu > Pyr-Phe > Pyr-Tyr. L-Pyrroli-donecarboxylyl-L-proline was not detectably hydrolyzed. The enzyme is apparently specific for the L-pyrrolidonecarboxylyl-L-amino acid optical isomers.

L8 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1968:84629 CAPLUS
DOCUMENT NUMBER: 68:84629
TITLE: Polypeptides. XXXIX. Elimination of the imidazole portion of histidine as an essential site for biological function of angiotensin
AUTHOR(S): Hofmann, Klaus; Andreatta, Rudolf H.; Buckley, Joseph P.; Hageman, William E.; Shapiro, Alvin P.
CORPORATE SOURCE: Univ. of Pittsburgh Sch. of Med., Pittsburgh, Pa., USA
SOURCE: J. Am. Chem. Soc. (1968), 90(6), 1654-5
CODEN: JACSAT
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 5-Valine-6-.beta.-(3-pyrazolyl)-L-alanine angiotensin II (I) in which the histidine residue at position 6 of 5-valine angiotensin II is replaced by the isosteric .beta.-(3-pyrazolyl)-L-alanine, exhibited surprisingly high pressor and myotropic activities. The pressor activity of I in pithed or nephrectomized rats and the myotropic activity in the guinea pig were 79, 57, and 52%, resp., that of 5-valine angiotensin II amide (angiotensinamide). The pressor activity in the nephrectomized rat of 5-valine-6-phenylalanine angiotensin II amide and 5-valine-6-lysine angiotensin II amide was 1 and 0.1%, resp., that of 5-valine angiotensin II amide. The pressor and myotropic activities of angiotensin do not depend on the characteristic acid-base properties of the imidazole ring. The stereo structure of the 5-membered heterocyclic ring of histidine and not its charge is apparently of crucial significance for high-level angiotensin activity. The acid-base character of imidazole appears to be of key significance in those situations where this ring system plays a direct role in a catalytic event. The Z-Asp-Arg-Val-Tyr-N3 (Z = PhCH2O2C) was coupled with ***Val*** - ***Pyr*** (3)-Ala-Pro-Phe-OBu-tert [Pyr(3) = .beta.-(3-pyrazolyl)] to give Z-Asp-Arg-Val-Tyr- ***Val*** - ***Pyr*** (3)-Ala-Pro-Phe-OBu-tert which was partially deblocked by exposure to CF3CO2H. The ensuing crude benzyloxycarbonyl octapeptide was purified by chromatog. on the ion exchanger AG-1 X2 and hydrogenolyzed to give I, [.alpha.]27D -47.5.degree. (c 0.29, 20% aq. dioxane).

L8 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1966:473866 CAPLUS

DOCUMENT NUMBER: 65:73866
ORIGINAL REFERENCE NO.: 65:13823[illegible],13824a-b
TITLE: Synthesis of D-Ser1-Nle4-(gal-NH2)25-.beta.-corticotropin(1-25), a highly potent analog of ACTH
AUTHOR(S): Boissonnas, R. A.; Guttmann, St.; Pless, J
CORPORATE SOURCE: Res. Lab. Pharm. Chem., Sandoz Ltd., Basel, Switz.
SOURCE: Experientia (1966), 22(8), 526
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Synthesis of a new analog of ACTH was described. It contains an amino-peptidase resistant D-serine residue at its amino end, a carboxy-peptidase resistant L-valinamide residue at its carboxyl end, and in position 4, an isologous norleucine residue. The pentaco-sapeptide was synthesized by methods known to avoid racemization. (Z = PhCH2O2C, Boc = tert-BuO2C, Trt = Ph3C, Nle = norleucyl throughout this abstr.) Z-Val-Gly-Lys(Boc)-Lys(Boc)-Arg(NO2)-Arg(NO2)Pro [m. 151.degree. (decompn.), [.alpha.]20D -38.degree. (MeOH)] was condensed with Val-Lys(Boc)-Val-Tyr-Pro-Val-NH2 [m. 142.degree. (decompn.), [.alpha.]20D -68.degree. (MeOH)] by the anhydride method to give Z-Val-Gly-Lys(Boc)-Lys(Boc)-Arg(NO2)-Arg(NO2)-Pro-Val-Lys(Boc)-Val-Tyr-Pro-Val-NH2, m. 190.degree. (decompn.), [.alpha.]20D -36.degree. (Me2NCHO). After elimination of the Z and NO2 groups by catalytic hydrogenation H-Val-Gly-Lys-(Boc)-Lys(Boc)-Arg-Arg-Pro-Val-Lys (Boc) - ***Val*** - ***Pyr*** - Pro - Val -NH2 [m. 191.degree. (decompn.), [.alpha.]20D -56.degree. (95:5 AcOH-H2O)] was obtained which, after conversion into the corresponding tritosylate, was coupled by the dicyclohexylcarbodiimide method with Trt-Glu(OBu-tert)-His(Trt)-Phe-Arg-Trp-Gly-Lys(Boc)-Pro [m. 209.degree. (decompn.), [.alpha.]20D -14.degree. (Me2NCHO)] into TrtGlu(OBu-tert)-His(Trt)-Phe-Arg - Trp - Gly - Lys(Boc) - Pro - Val Gly-Lys(Boc)Lys (Boc)-Arg-Arg-Pro-Val-Lys(Boc)-Val-Tyr- Pro- Val-NH2.3 (p-MeC6H4SO3H), m. 184.degree. (decompn.), [.alpha.]20D -53.degree. (MeOH). After selective elimination of the .alpha.-Trt groups the resulting peptide, m. 170.degree. (decompn.), [.degree.]20D -50.degree. (MeOH), was condensed with Boc-D-Ser-Tyr-Ser-Nle-N3 (prepd. from the corresponding hydroxide), m. 211.degree., [.alpha.]20D 8.degree. (MeOH), into Boc-D-Ser-Tys-Ser-Nle-Glu (OBu-tert)-His(Trt)-Phe-Arg - Trp - Gly - Lys (Boc)-Pro-Val-Gly-Lys (Boc)-Lys(Boc)-Arg - Arg - Pro - Val - Lys (Boc)-Val-Tyr-Pro-Val-NH2.3(p-MeC6H4SO3H), m. 198.degree. (de(compn.), [.alpha.]20D -36.degree. (95:5 AcOH-H2O). After cleavage of all protecting groups by trifluoroacetic acid and treatment with IRA-410 in the acetate form, the free pentacosapeptide was obtained as dodecaacetate decahydrate in analytically pure state (m. 172.degree., [.alpha.20D 74.degree.; N acetic acid). The high and hitherto unsurpassed level of corticotropic activity exhibited by this pentacosapeptide (about 625 I.U./mg. free base), both in the rat and in human, is remarkable.

L8 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1965:439409 CAPLUS
DOCUMENT NUMBER: 63:39409
ORIGINAL REFERENCE NO.: 63:7103a-f
TITLE: Peptide syntheses by using O-(Cbo-aminoacyl)oximes and O-(Cbo-aminoacyl)pyrazolone enols
AUTHOR(S): Losse, Guenter; Hoffmann, Karl Heinz; Hetzer, Gudrun
CORPORATE SOURCE: Univ. Halle, Germany
SOURCE: Ann. Chem. 684 (1965) 236-42
DOCUMENT TYPE: Journal
LANGUAGE: German

GI For diagram(s), see printed CA Issue.

AB Enol esters of N-protected amino acids with 3-nitroacetophenoxime (I) and 1-phenyl-3-methyl-5-pyrazolone (III) were prepd. by using the carbodiimide or the chloroformic acid ester method. Method A: To 0.02 mole of N-protected amino acid in abs. 30 ml. tetrahydrofuran (THF) and 0.02 mole abs. Et3N, was added at -15.degree., 0.02 mole ClCO2Et. After standing for 0.5 hr. at -15.degree. the mixt. was treated with 0.02 mole I or II in abs. THF and stirred for 1 hr. at -15.degree. and for 12 hrs. at 18.degree.. The solvent was evapd., and the residue dissolved in AcOEt, washed with 5% NaHCO3, dried over Na2SO4, and repptd. with petroleum ether. Method B: N-Protected amino acid (0.02 mole) and 0.02 mole I or II in 50 ml. abs. CH3CN was mixed, at 15.degree., with 0.02 mole dicyclohexyl-carbodiimide in 10 ml. abs. CH3CN and let stand for 3 hrs. at -15.degree., and 12 hrs. at room temp. The urea was filtered off, the solvent evapd. in vacuo, and the residue dissolved in AcOEt, washed with N

HCl, H2O, and 5% NaHCO3, dried over Na2SO4, concd. in vacuo, and pptd. with petroleum ether. The cptd. I or II was removed by heating at 60.degree./106 mm. for some hrs. The following compds. were prepd. (Cbo = PhCH2O2C, ox = 3-O2NC6H4CMe:NO, NPS = 2-O2NC6H4S) [method, m.p., [.alpha.]20D (solvent) given]: Cbo-Gly-pyr, A, B, 132.degree., -; Cbo-DL-Ala-ox, A, 80-2.degree., -; Cbo-DL-Ala-ox, A, 100.degree., -27.6.degree. (Me2CO); Cbo-DL-Ala-pyr, A, B, 119-20.degree., -; Cbo-L-Ala-pyr, A, 108-19.degree., -22.0.degree. (AcOEt); Cbo-DL-Val-ox, A, 79-81.degree., -; Cbo-L-Val-ox, A, 86-7.degree., -15.5.degree. (Me2CO); Cbo-DL- ***Val*** - ***pyr*** , A, B, 94.degree., -; Cbo-L- ***Val*** - ***pyr*** , A, 83-4.degree., -24.5.degree. (EtOH); Cbo-DL-Leu-pyr, A, 61-2.degree., -; Cbo-DL-Phe-ox, A, 87.degree., -; Cbo-L-Phe-ox, A, 110.degree., -5.0.degree. (Me2CO); Cbo-DL-Phe-pyr, A, b, 114.degree., -; Cbo-L-Phe-pyr, A, B, 137-8.degree., -19.5.degree. (EtOH); Cbo-L-S-Bz-Cys-ox, A, amorphous, -20.8.degree. (Me2CO); Cbo-L-S-Bz-Cys-pyr, A, amorphous, -13.1.degree. (AcOEt); Cbo-L-Asp-.alpha.-OBz, A, 88-9.degree., -18.2.degree. (Me2CO); Cbo-L-Glu-.alpha.-OBz-.gamma.-pyr, A, 85-6.degree., -3.25.degree. (pyridine); Di Cbo-L-Lys-ox, A, amorphous, -29.4.degree. (Me2CO); Di-Cbo-L-Lys-pyr, A, 100-1.degree., -26.2.degree. (pyridine); Cbo-L-Phe-L-Ala-ox, A, 154-5.degree., -4.60.degree. (Me2CO); Cbo-L-Val-L-Ala-pyr, A, 105-6.degree., -28.1.degree. (EtOH); NPS-L-Phe-ox, B, 123-4.degree., -80.6.degree. (Me2CO); NPS-L-PheOH, -, 134-5.degree., -47.7.degree. (THF). The Cbo group was selectively removed only in the case of the pyrazolone enol esters (with 33% HBr-AcOH). In the case of oxime esters the Cbo was not selectively removed but the NPS could be removed by 3 equivs.HCl in AcOEt. The following free amino acid esters were prepd. (m.p. and [.alpha.]20D given); Gly-pyr.2HBr, 157-9.degree., - DL- ***Val*** - ***pyr*** .2HBr, 134-6.degree., -; L- ***Val*** - ***pyr*** .2HBr, 196-8.degree., 7.5.degree. (EtOH); DL-Phe-pyr.2HBr, 140-2.degree., -; L-Phe-ox.HCl, 170.degree., 33.8.degree. (EtOH). The N-protected esters were coupled either with the Et3N salts of free amino acids in dioxane-H2O or with their ethyl esters in THF or CH3CN to give the following peptides: (% yield, m.p., and [.alpha.]20D in EtOH given): Cbo-Phe-Ala, 54, 158-60.degree., -10.6.degree.; Cbo-Ala-Phe, 50, 176-8.degree., 19.4.degree.; Cbo-Cys(S-Bz)-Gly-OEt, 73, 100-2.degree., -35.5.degree. (MeOH); Di-Cbo-Lys-Phe-OEt, 88,130-1.degree., -43.7.degree.; Cbo-Gly-Phe-Gly-OEt, 89, 117-19.degree., -11.8.degree.; Cbo-Ala-Phe-Gly-OEt, 84, 184-5.degree., -35.0deg; (CHCl3); Cbo-Phe-Ala-Phe-Gly-OEt, 60, 187-9.degree., -34.9.degree. (Me2CO); Cbo-Val-Ala, 60, 179.degree., -19.5.degree.; Cbo-Phe-Val, 60, 145-6.degree., -16.0.degree.; Cbo-Gly-Phe, 73, 127-8.degree., 38.2.degree.; Cbo-Ala-Phe, 64, 121-2.degree., 66.7.degree. (N HCl); Cbo-Cys(S-Bz)-Gly-OEt, 72, 99-100.degree., -26.9.degree. (AcOH). The racemization during coupling was studied by the Anderson-Young test. It was found that in oximes there is racemization up to 21% (in the cases studied), but no racemization was observed in the case of pyrazolone enols.

=> d his

(FILE 'HOME' ENTERED AT 14:41:12 ON 20 MAY 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 14:41:55 ON 20 MAY 2002

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L1          5851 S (DIPEPTIDYL PEPTIDASE IV) OR (DP-IV) OR (DPP-IV)
L2          1752 S L1 (P) INHIBIT?
L3            14 S L2 (P) UNSTABLE
L4             5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)
L5             5 S (ILE-THIA) OR (ILE-PYR) OR (VAL-THIA) OR (VAL-PYR)
L6             5 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)
L7             0 S L6 (P) L1
L8             5 S L6 NOT L4

=> s alkylketone or (fluoroalkyl ketone) or (chloroalkyl ketone) or (dipeptid? cyanide) or (pyridi
L9           166 ALKYLKETONE OR (FLUOROALKYL KETONE) OR (CHLOROALKYL KETONE) OR
                 (DIPEPTID? CYANIDE) OR (PYRIDIUM METHYLKETONE)

=> s l1 and l9
L10            0 L1 AND L9
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=> s l9 and dipeptid?
L11           1 L9 AND DIPEPTID?

=> d l11 not l4
L4 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> s l11 not l4
L12           1 L11 NOT L4

=> d l12 1 ibib abs

L12  ANSWER 1 OF 1  SCISEARCH  COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER:    78:95513  SCISEARCH
THE GENUINE ARTICLE: EP971
TITLE:               STERIC EFFECTS ON REACTION OF TRIETHYLENETETRAMINE WITH
                     NICKEL(II)-  ***DIPEPTIDEAMIDE***  -  ***CYANIDE***
                     COMPLEXES
AUTHOR:              PAGENKOPF G K (Reprint); MARCHESE W A
CORPORATE SOURCE:    MONTANA STATE UNIV, DEPT CHEM, BOZEMAN, MT, 59715
                     (Reprint)
COUNTRY OF AUTHOR:   USA
SOURCE:              JOURNAL OF COORDINATION CHEMISTRY, (1978) Vol. 7, No. 4,
                     pp. 249-252.
DOCUMENT TYPE:       Article; Journal
FILE SEGMENT:        PHYS
LANGUAGE:            ENGLISH
REFERENCE COUNT:     17


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     (FILE 'HOME' ENTERED AT 14:41:12 ON 20 MAY 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     14:41:55 ON 20 MAY 2002
L1          5851 S (DIPEPTIDYL PEPTIDASE IV) OR (DP-IV) OR (DPP-IV)
L2          1752 S L1 (P) INHIBIT?
L3            14 S L2 (P) UNSTABLE
L4             5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)
L5             5 S (ILE-THIA) OR (ILE-PYR) OR (VAL-THIA) OR (VAL-PYR)
L6             5 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)
L7             0 S L6 (P) L1
L8             5 S L6 NOT L4
L9           166 S ALKYLKETONE OR (FLUOROALKYL KETONE) OR (CHLOROALKYL KETONE) O
L10            0 S L1 AND L9
L11            1 S L9 AND DIPEPTID?
L12            1 S L11 NOT L4

=> d l2 (p) diabetes
'(P)' IS NOT A VALID FORMAT
'DIABETES' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):end

=> s l2 (p) diabetes
L13         158 L2 (P) DIABETES

=> duplicate remove l13
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L13
L14           66 DUPLICATE REMOVE L13 (92 DUPLICATES REMOVED)

=> s l9 and l14
L15            0 L9 AND L14

=> d his
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     (FILE 'HOME' ENTERED AT 14:41:12 ON 20 MAY 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     14:41:55 ON 20 MAY 2002
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L3            14 S L2 (P) UNSTABLE
L4             5 DUPLICATE REMOVE L3 (9 DUPLICATES REMOVED)
L5             5 S (ILE-THIA) OR (ILE-PYR) OR (VAL-THIA) OR (VAL-PYR)
L6             5 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)
L7             0 S L6 (P) L1
L8             5 S L6 NOT L4
L9           166 S ALKYLKETONE OR (FLUOROALKYL KETONE) OR (CHLOROALKYL KETONE) O
L10            0 S L1 AND L9
L11            1 S L9 AND DIPEPTID?
L12            1 S L11 NOT L4
L13          158 S L2 (P) DIABETES
L14           66 DUPLICATE REMOVE L13 (92 DUPLICATES REMOVED)
L15            0 S L9 AND L14

=> s l13 and masked
L16            0 L13 AND MASKED

=> s l9 and diabetes
L17            0 L9 AND DIABETES

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     (FILE 'HOME' ENTERED AT 14:41:12 ON 20 MAY 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     14:41:55 ON 20 MAY 2002
L1          5851 S (DIPEPTIDYL PEPTIDASE IV) OR (DP-IV) OR (DPP-IV)
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L5             5 S (ILE-THIA) OR (ILE-PYR) OR (VAL-THIA) OR (VAL-PYR)
L6             5 DUPLICATE REMOVE L5 (0 DUPLICATES REMOVED)
L7             0 S L6 (P) L1
L8             5 S L6 NOT L4
L9           166 S ALKYLKETONE OR (FLUOROALKYL KETONE) OR (CHLOROALKYL KETONE) O
L10            0 S L1 AND L9
L11            1 S L9 AND DIPEPTID?
L12            1 S L11 NOT L4
L13          158 S L2 (P) DIABETES
L14           66 DUPLICATE REMOVE L13 (92 DUPLICATES REMOVED)
L15            0 S L9 AND L14
L16            0 S L13 AND MASKED
L17            0 S L9 AND DIABETES

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